Allergy Abstracts

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Asthma and Hay Fever

Variants of Kartagener's Syndrome in the Same Family. Overholt, E. L., and Bauman, D. F.: Ann. Int. Med. **48**: 574, 1958.

Kartagener's syndrome consists of the triad of situs inversus, bronchiectasis, and chronic sinusitis. The clinical course of the syndrome is characterized by nasal discharge, frequent colds, and chronic bronchitis in early infancy. At least 90 per cent of the patients manifest symptoms prior to the age of 14 years. There is usually a history of repeated episodes of pneumonia. Asthma, emphysema, bronchiectasis, nasal polyposis, pulmonary osteoarthropathy, and cor pulmonale are eventual complications. The incidence of bronchiectasis in persons with situs inversus or dextrocardia varies from 12 to 23 per cent as contrasted with an incidence of 0.03 to 0.5 per cent encountered in the general hospital and clinical population. Situs inversus itself occurs in approximately one of 6,000 to 8,000 persons. All cases of Kartagener's syndrome do not present the classical symptoms. Probable cases of

this syndrome have been reported with agenesis of the sinuses without evidence of sinusitis, as well as with sinusitis without evidence of bronchiectasis. Profuse nasal discharge and expectoration of large amounts of mucous secretions are common, as is nasal polyposis. The bronchiectasis seen in this condition is tubular rather than cystic and appears to be of the acquired type. There appears to be a definite familial tendency. In children presenting chronic respiratory symptoms one must consider, in addition to allergy and infection, such causes as congenital heart disease with increased pulmonary blood flow, abnormalities of the great vessels with an aortic ring or anomalous retro-esophageal artery, Kartagener's syndrome, agammaglobulinemia, and chronic cystic disease of the pancreas. H. F.

A New Xanthine Derivative: Theophylline With Diethylenediamine. Cass, L. J., and Frederik, W. S.: New York J. Med. **58**: 2391, 1958.

The authors treated 43 cases of bronchial asthma and 64 cases of cardiac asthma with theophylline combined with diethylenediamine as the solubilizing agent. Patients were given enteric-coated tablets, each containing 200 mg. of theophylline and 50 mg. of diethylenediamine. Cross-over controls with the use of placebos were tried, but the sustained effect of the medication, when effective, often prevented a fair comparison. Early in the study, patients were given either one or two tablets of the xanthine derivative every four hours. Since it soon became apparent that one tablet was almost as effective as two tablets, the standard dose eventually adopted was one tablet 3 or 4 times daily. Eighteen patients with subacute asthma obtained essentially complete relief while on this medication. Another 10 asthmatic patients showed moderate improvement, 9 showed slight improvement, and 7 experienced no relief following this medication. The medication did not help the chronic fibrotic asthma patients in the group. In this study, theophylline with diethylenediamine was shown to be an effective bronchodilator in a high percentage of cases of bronchial asthma. It proved to be less effective in the cardiac cases. R. W.

Increased Effect of Adrenalin After Pretreatment With ACTH and Prednisone in Cases of Bronchial Asthma. Dunér, H.: Acta med. scandinav. **159**: 243, 1957.

Five patients with severe asthma which failed to respond to epinephrine, 0.4 to 0.8 mg., were treated with steroids. While the patients were under steroid treatment, Adrenalin, 0.4 mg., was effective in controlling asthmatic attacks. It is postulated that "these hormones potentiate the bronchiolytic effect of Adrenalin." E. K.

Urinary Excretion of Histamine in Bronchial Asthma. Dunér, H., and Pernow, B.: Acta med. scandinav. **161**: 361, 1958.

Urine samples from ten adult asthmatic patients were assayed for histamine content by a method using an ion exchange column, followed by elution of histamine from this column, and bioassay. In 8 cases no free histamine was found in urine collected during acute asthmatic attacks; in 2 cases only trace amounts were found. When asthma had subsided, histamine excretion increased to values typical of normal persons or slightly above (in one case) normal limits. Determinations of urinary conjugated histamines were carried out in 2 patients, and these substances were also found to be decreased during asthmatic attacks. A histamine inhibitor was found in 3 urine specimens

collected during acute asthma. This inhibitor was not present when the subject was free of asthma, and its nature is unknown. The findings are discussed and it is noted that the results are at variance with those reported by Rose, who found histamine excretion much increased during an attack. E. K.

Anaphylaxis

Effect of Hydrocortisone on Activation and Activity of Anaphylatoxin In Vitro. Hershberger, L. G., and Hansen, L. M.: Proc. Soc. Exper. Biol. & Med. **98**: 150, 1958.

The physiologic importance of anaphylatoxin, which occurs naturally in the blood of man and certain animals, has not been clarified. It has been shown that incubation of plasma at 37° C. with agar or similar polysaccharides activates the anaphylatoxin to become a potent histamine releaser, thereby effecting contraction of the isolated guinea pig muscle. Tachyphylaxis, which results from the repeated administration of anaphylatoxin, is believed to result from exhaustion of the stored histamine in the muscle. Studies were conducted to determine the effects of hydrocortisone on the activity and activation of anaphylatoxin in vitro.

Plasma was obtained from Sprague-Dawley rats under standard conditions and assayed against guinea pig ileum. For testing purposes, aliquots of the plasma were treated as follows: "(1) diluted 1:1 with saline as a control; (2) activated by mixing 1:1 with 0.1 per cent agar solution; (3) activated with agar in the presence of hydrocortisone-hemisuccinate or equivalent amount of neutralized succinic acid; (4) mixed with hydrocortisone-hemisuccinate or neutralized succinic acid, without agar, as another control." After incubation at 37° C. for ten minutes, portions of these mixtures were transferred to tissue bath so that the effect on isolated guinea pig ileum could be observed.

Activation of anaphylatoxin in vitro was inhibited by the presence of 1.25 mg./ml. hydrocortisone-hemisuccinate in the incubation media. Succinic acid alone did not produce the inhibition. A concentration of 1.25 mg./ml. of hydrocortisone-hemisuccinate in the tissue bath also clearly inhibited the responsiveness of the guinea pig ileum not only to anaphylatoxin but also to exogenous histamine, acetylcholine, and bradykinin. Contractions occurred again when the hydrocortisone was removed from the mixture. Tachyphylaxis produced by anaphylatoxin alone was not inhibited by hydrocortisone. The inhibition, therefore, was probably due to nonspecific desensitization of the muscle to histamine rather than to interference with anaphylatoxin or histamine release. H. Stryker

Anaphylaxis and the Nervous System. Part III. Filipp, G., and Szentivanyi, A.: Ann. Allergy **16**: 306, 1958.

In a previous paper it had been shown that anaphylactic shock could be abolished or markedly interfered with by prior production of bilateral focal lesions of the tuberal region of the hypothalamus. The present paper concerns itself with an attempt to determine whether the production of antibodies and/or the union of antigen and antibodies in the tuberal-injured animal is affected by this procedure.

Guinea pigs which had been subjected to the Horsley-Clarke stereotaxic technique were sensitized subcutaneously with bovine serum globulin on the seventh day after operation. The sensitizing injections were repeated twice at two-day intervals. On the seventeenth day after the last sensitizing dose,

the animals were bled and Schultz-Dale experiments were performed. Of 49 animals examined by the Schultz-Dale technique, only 5 showed positive results and 44 were negative, whereas in a group of 35 animals serving as controls, 26 Schultz-Dale reactions were positive and only 8 were negative. In a second group of guinea pigs subjected to operation and sensitized with undiluted horse serum, precipitin ring tests done with serum obtained 14 days after sensitization revealed a marked reduction in the precipitate in the tuberal-injured group as compared to the control group. In a series of passive transfer experiments in which 20 guinea pigs served as donors and 20 as recipients, 10 of the donor guinea pigs were subjected to destruction of the tuberal region. On the seventh postoperative day, these animals were sensitized along with 10 control animals by the subcutaneous injection of 0.3 ml. of undiluted horse serum. On the fourteenth day following sensitization, both groups of animals were bled and the sera were used to sensitize 20 normal guinea pigs. Twenty-four hours later a challenging intravenous dose of 0.5 to 1.0 ml. of homologous antigen was administered. The sera derived from tuberal-injured animals failed to sensitize 8 of the 10 recipients, whereas all 10 of the animals sensitized with sera from the control group reacted positively. All three of the experiments, therefore, indicated that the production of antibodies in tuberal-injured guinea pigs is greatly diminished. Previously reported experiments, however, have shown that anaphylactic reactivity is diminished in animals sensitized prior to the operative procedure, thus indicating that antibody production per se is not the important factor involved. "For this, two alternative explanations are available: (1) the production of antibodies in previously sensitized tuberal-injured animals is inhibited and the antibodies existing prior to tuberal lesion had been metabolized; (2) the inhibition of the production of antibodies is not the only way by which tuberal lesions interfere with the anaphylactic mechanism." In an effort to determine which of these mechanisms effected shock, a series of guinea pigs was sensitized subcutaneously with undiluted horse serum, another group of nonsensitive guinea pigs was subjected to the tuberal injury, and another group served as a control. The guinea pigs in the sensitized group were bled on the fourteenth day following sensitization, and the tuberal-injured animals were sensitized intraperitoneally with 3 ml. of the serum of each of the donors. Twenty-four hours following passive sensitization the animals were challenged by intravenous injection of 1.0 ml. of homologous antigen. Of 13 tuberal-injured animals, 11 showed no shock and one reacted with severe shock.

Two rabbits were then immunized by four intravenous injections of undiluted horse serum at 3-day intervals. Fifteen days following sensitization the precipitin level of the rabbit serum was shown to be 1 to 2,560 by ring test. The serum of these rabbits was used to passively sensitize 11 tuberal-injured and 10 control guinea pigs. A challenging dose of antigen produced 2 lethal reactions and 3 mild reactions in the 11 tuberal-injured animals. Of the 10 control animals, 9 died of acute shock and only one survived after a fairly severe shock, thus indicating that bilateral focal lesions of the tuberal region inhibit not only active but also passive anaphylactic shock. Further experiments carried out with rabbits showed that tuberal-injured animals were definitely less susceptible to shock than normal animals. Both tuberal-injured animals and control animals had high titers of precipitin before provocation of shock. This precipitin level declined after shock to the same degree in both the tuberal-injured animals and a control group. Tuberal-injured guinea pigs which had been sensitized prior to the operative procedure and had failed to respond to challenging doses of antigen with any signs of

anaphylactic shock were killed. One hour following this challenging shock Schultz-Dale experiments were carried out on the intestinal strips. In no case did any of the strips respond by contraction following addition of the antigen. When the same experiments were expanded to include a larger number of animals, the intestinal strip of only one of 10 tuberal-injured animals responded to the addition of antigen. The intestinal preparations of control animals gave positive reactions in 2 of 10 cases. These findings point to the conclusion that antibody production is significantly reduced in tuberal-injured guinea pigs. H. F.

Miscellaneous Allergies

Fatal Reactions to Penicillin: Evaluation of a Test for Sensitivity. Smith, V. M.: New England J. Med. **257**: 447, 1957.

Procaine-penicillin solution containing 300,000 units per milliliter was employed for scratch testing and conjunctival testing of 1,365 adults. Of these, 567 persons collected at random at an Army dispensary among patients, dispensary personnel, visitors, and associates were employed as the control group. The results of the tests in this group could not be correlated with anaphylactic reactions to penicillin. The second group consisted of 798 subjects who were to receive penicillin therapy at an Army hospital. In addition, there were 7 patients who had recently been brought to the Army hospital because of acute anaphylactic reactions to penicillin. Of the 1,365 subjects interviewed, 64 (4.7 per cent) gave a history of previous sensitivity reactions to penicillin. Of these, 48 (78 per cent) had delayed urticarial reactions, 4 (6 per cent) had reactions of the serum sickness type manifested by fever, urticaria, and joint inflammation, and 12 (18 per cent) had anaphylactic collapse within minutes following a penicillin injection. Seven of the patients with a history of recent anaphylactic reactions had been referred to the hospital from outside facilities and, therefore, were samples of an untested group. The actual proportion of history of anaphylactic reactions among the group was 5:57, or 8.7 per cent of penicillin sensitivity reactions. Of 1,365 subjects tested with full-strength penicillin, one subject had a systemic reaction to the tests. This occurred in a person who had previously received penicillin without untoward effect. He showed positive test responses. His reaction was controlled by 0.3 ml. of a 1:1,000 solution of epinephrine. In the control group, areas of erythema 1.0 cm. or less in diameter developed in 99 per cent. The remaining 1 per cent of the group developed areas of erythema that measured 1.3 to 1.6 cm. in diameter. Two of these subjects had wheals measuring 0.5 and 0.7 cm., respectively, and positive eye tests. One of these subjects had had a severe anaphylactic shock following a penicillin injection two days before he was tested. Another subject in the control group had itching and edema of the eye but no skin reaction. A week after the positive eye test he consulted a private physician, received an injection of penicillin, and died in acute anaphylactic shock. On the basis of these results, it was decided that development of an area of erythema measuring more than 1 cm. in diameter, a wheal, or both within 20 minutes and a positive eye test within 20 minutes were to be considered positive responses. By this criterion, 1.1 per cent of 1,365 subjects tested showed positive responses. Ten patients in this series were known to have had anaphylactic reactions to penicillin, one of which was fatal. Intramuscular injections of 600,000 units of procaine penicillin were administered to 778 patients in the second group immediately after they demonstrated negative

test responses. One patient had a mild anaphylactic reaction a few minutes after the injection, manifested by tachycardia, palpitation, dyspnea, and apprehension. This was controlled by epinephrine administered subcutaneously. There were no immediate sensitivity reactions among the other patients. Of the seven patients who had been brought to the hospital because of recent acute anaphylactic reactions to penicillin injections, all responded with positive scratch and eye tests, even though each was receiving full therapeutic doses of antihistaminic agents. Each of 12 subjects who gave a history of previous anaphylactic reaction to penicillin also manifested positive test responses, except for two whose reactions had occurred 18 and 39 months before the tests. The others had experienced their reactions within a few days of the tests. The exceptions suggested the possibility that anaphylactic susceptibility is transient and that persons who recover from anaphylactic reactions to penicillin can, after an appropriate time, safely receive the drug again. It was suggested that the testing procedure described should be applied routinely to all patients scheduled to receive penicillin before the first injection of a series. E. W.

Acute Vascular Purpura Following Immunization With Asiatic Influenza Vaccine. Stefanini, M., Piomelli, S., Mele, R., Ostroski, J. T., and Colpoys, W. P.: New England J. Med. **259**: 9, 1958.

A 37-year-old woman received 1 ml. of polyvalent influenza vaccine intracutaneously into each deltoid area. Three days later she developed blepharoconjunctivitis and soreness of the mouth and throat which did not respond to antihistamine therapy. There was no history of allergy to foods, drugs, or previous injections. Within a week she developed generalized purpura with vasculitis of the skin, mucous membranes, and kidneys. The clinical picture closely resembled that of serum sickness. Local areas of indolent necrosis were evident at both injection sites. Neither white nor red cell antibodies could be demonstrated in the patient's serum, but platelet agglutinins were present in significant titers. Symptoms were controlled by the administration of ACTH and steroids.

Attempts to detect blood vessel wall antibodies in the patient's serum were unsuccessful. Moreover, no antibodies against allantoic fluid were found. However, positive complement fixation, precipitation, and hemagglutinin inhibition tests were noted against influenza type-A virus vaccine with the patient's serum and with the serum of immunized controls. Reinjection of dilute vaccine in small amounts subcutaneously into this patient resulted in the production of local vascular purpura, which histologically was characterized by perivascular infiltration, vascular dilatation, and endothelial swelling. Passive transfer of this reaction was demonstrated after the intracutaneous administration of 0.1 ml. amounts of the patient's serum into the skin of nonimmunized volunteers. Normal serum, saline, and vaccine controls were negative. The patient's skin failed to respond to patch tests with undiluted vaccine and to intracutaneous tests made with egg white, egg yoke, or the thimerosal preservatives in the vaccine.

The close similarity between these pathologic findings and those found in anaphylactoid purpura is discussed, and the resemblance of the local lesion to an Arthus phenomenon is pointed out. The authors suggest the possibility that, following the introduction of the vaccine, antibodies were formed against the virus protein, which, presuming the presenceof retained antigen, resulted in a local and general antigen-antibody reaction in this patient. H. Stryker

Severe Allergic Reaction to Poliomyelitis Vaccine. Kaufman, R. E., and Janeway, M.: New York J. Med. **58**: 2832, 1958.

Nine hours following her third poliomyelitis inoculation, a 20-year-old student nurse developed a severe reaction which was manifested by intense urticaria and angioedema of the eyelids. A few days later she complained of paresthesias as well as edema of the left forearm, and at that time neurologic examination revealed slight weakness of the left hand grip and slight hypalgesia of the outer aspect of the left forearm. The injection had been given in the left arm. She failed to respond to antihistamines and was hospitalized, at which time her therapy was supplemented with 30 mg. of prednisone daily. She continued to have symptoms primarily in the left arm but also developed some muscle tenderness and arthralgia in the right thigh. Examination by a neurologist three weeks following the polio inoculation showed some winging of the left scapula, weakness of the left hand grip, diminution of the biceps reflex, and marked tenderness of the nerve trunks and brachial plexus trunks on the left side. No objective sensory changes were observed, and a diagnosis of serum radiculitis was made. Five weeks later, despite continued steroid and antihistamine therapy, urticaria, angioedema, and arthralgia with periodic temperature elevations still persisted. Her symptoms completely subsided in about 9 weeks, at which time all her medication was stopped. Follow-up examination 6 months later showed completely normal findings. Laboratory tests performed during hospitalization were all essentially normal except for a leukocytosis as high as 19,000 with 80 per cent polys during the acute phase of her illness. No eosinophil counts were reported. The patient had a negative past and personal allergic history and had received no drugs or injection for many months prior to the present illness. She had had penicillin on a number of occasions 8 years previously without any untoward reaction. Passive transfer studies performed at the height of the patient's illness on one recipient gave completely negative reactions to horse serum 1:100, crystalline penicillin G 50,000 units per cubic centimeter, streptomycin sulfate 0.05 Gm. per cubic centimeter, and undiluted Salk vaccine.

After recovery, direct skin tests with horse serum 1:1,000, crystalline penicillin G 10,000 units per cubic centimeter, streptomycin sulfate 0.005 Gm. per cubic centimeter, and Salk vaccine 1:100 gave negative reactions. Precipitin tests against monkey kidney antigen carried out on serum drawn 4 and 7 weeks following the onset of the illness were also negative. Electrophoretic studies done on these two sera showed normal albumin but slightly elevated alpha-2 and gamma globulins. The authors state that their findings have failed to prove which antigenic component in the vaccine was the etiological excitant. R. W.

Penicillinase Treatment of Acute Renal Insufficiency Due to Penicillin Hypersensitivity. Unger, A. M., and Nemuth, H. I.: J. A. M. A. **167**: 1237, 1958.

A 65-year-old man with cellulitis of the leg was given 400,000 units of procaine penicillin G, 0.5 Gm. of dihydrostreptomycin-penicillin (Combiotic) twice a day, and 250 mg. per day of Benadryl in divided doses. The leg began to improve rapidly, but on the third hospital day the patient became restless, confused, and uncooperative. The urinary output began to fall, and anuria was present on the seventh hospital day. Urinalysis showed marked albuminuria and hematuria. An urticarial reaction appeared on the thighs and spread rapidly over the entire body. There was severe pruritus. Steroids

were administered but failed to alter the rapid deterioration of the patient's condition. At the height of the oliguria, he was given a single intramuscular injection of 800,000 units of penicillinase. Prednisone therapy was continued. Eight hours after the administration of penicillinase, the urine output was 50 c.c., but within the next 24 hours the urine volume was over 1 liter. The patient's clinical condition improved considerably, and the skin lesions began to fade within 24 hours following administration of the penicillinase. The authors regard this as a case of acute renal failure and exfoliative dermatitis caused by penicillin which responded to a specific therapeutic agent, penicillinase. M. C.

Penicillinase-Proved Allergy to Penicillin in Poliomyelitis Vaccine. Zimmerman, M. C.: J. A. M. A. **167**: 1807, 1958.

Six patients who developed skin reactions from 1 to 21 days following the injection of 1 c.c. of poliomyelitis vaccine were studied. The lesions consisted of severe urticaria, bullous lesions, or peculiar nummular plaques which oozed. Most of the patients were treated with steroids and local agents, without relief. In each instance the injection of 800,000 units of penicillinase produced dramatic clearing of the lesions, usually within 24 hours. Subsequently, these patients were given Wyeth poliomyelitis vaccine which contains less than 0.001 units of penicillin per cubic centimeter. No reactions occurred following the administration of this vaccine. It was noted that all other brands of poliomyelitis vaccine contain from 1 to 200 units of penicillin per cubic centimeter. Since even this small amount of penicillin can produce allergic reactions in highly susceptible patients, it was concluded that the skin reactions in these six patients were caused by the penicillin in the vaccine, especially since the lesions cleared rapidly following the injection of penicillinase. The absence of reactions in these patients following the injection of a brand of penicillin-free vaccine was considered to be proof that other allergens in the poliomyelitis vaccine had not caused the reactions. It was stressed that penicillin-free vaccines should be used in patients with a history of penicillin sensitivity. If this is not possible, penicillinase should be given prophylactically preceding the vaccine injection. M. C.

Does Honey in Infant Feeding Cause Allergy? Strem, E. L., and Stoesser, A. V.: Ann. Allergy **16**: 375, 1958.

Honey, a good source of carbohydrate for infant feeding, is known to produce better average weekly weight gains, linear growth measures, and hemoglobin values than Karo syrup and is said to cause fewer gastrointestinal problems. In spite of this, it has not been extensively employed for infant feeding. In the past, certain investigators have suspected that honey could be the cause of sensitivity reactions in children as well as in adults. Honey contains protein from both insect and plant sources as well as resins, gums, beeswax, coloring matter, volatile oils, etc., any and all of which could perhaps be antigenic in nature. In addition, a considerable amount of pollen is found in honey. Examination of honey obtained from a common source in Minnesota revealed that unstrained honey contained appreciable numbers of pollen granules of sweet clover, alfalfa, and white clover plus a few others in minimal amounts.

Fifty-two infants, averaging about 5 months of age, were fed honey as a carbohydrate supplement in their formulas and were observed for an average period of twenty weeks. Of the 52 infants, 24 had a positive family history of allergy. Four babies started the study with an existing allergic condition (eczema), and two of these had a family history of allergy. At the

end of 20 weeks, it was noted that in the group of infants with a family background of allergy, 9 had developed either eczema or wheezing. This was in addition to the two in whom allergic disease existed before honey was added to the formula. In the other group, 6 developed similar types of allergic manifestations. No gastrointestinal complaints were noted in any of the children. Those infants who had shown allergic manifestations were then skin tested with unstrained honey, honey strainings, and the pollens present in the honey. No positive skin reactions were observed in the entire group. There were three infants in whom honey was suspected as the cause of trouble since they improved when the honey was discontinued. It is concluded that honey is not an important cause of allergic manifestations in infants. H. F.

Coexistence of Intussusception and Henoch's Purpura. Steinhardt, I. D., and Jonas, A. F.: New England J. Med. **257**: 553, 1957.

The coexistence of intussusception and Henoch's purpura was observed in a 5-year-old girl who developed an ecchymotic rash and swelling of the knees and ankles two days following a tetanus toxoid injection. There was a history of a similar but less severe reaction following a diphtheria-pertussis-tetanus injection 2 years previously. On examination, the abdomen was found to be tender but not distended. The right inguinal region was tender, swollen, and bluish, and both thighs and gluteal regions were ecchymotic. On the second hospital day, the patient passed a grossly bloody urine. She vomited and went into shock. During the next few days supportive therapy and other measures produced only slight improvement. On the eighth hospital day, her condition suddenly became worse; there was more vomiting and distention, and films of the abdomen showed mechanical obstruction with absence of gas in the colon. At laparotomy a gangrenous ileoileal intussusception, 15 cm. in length, was found and a resection was done with an end-to-end anastomosis. The patient withstood the procedure well and was discharged 12 days later. The mechanism of intussusception in purpura is generally thought to be due to an intramural hematoma of the intestinal wall acting as a tumor and providing a leading point of peristaltic invagination. Other complications of abdominal purpura include appendicitis, duodenal perforation, and intestinal obstruction due to cicatrization. Intussusception, a rare complication of Henoch's purpura, must constantly be borne in mind in the presence of this condition, since early surgery is definitely indicated. E. W.

Anaphylactic Shock From a Penicillin Lozenge. Gullatt, R.: New England J. Med. **257**: 1037, 1957.

A 55-year-old man who had had a previous episode of anaphylactic shock following an injection of penicillin collapsed within five minutes following the ingestion of a penicillin lozenge. The administration of large doses of epinephrine, steroids, and other supportive measures was required to save his life. E. W.

Untoward Reactions to Benzathine Penicillin G in a Study of Rheumatic-Fever Prophylaxis in Adults. Hsu, I., and Evans, J. M.: New England J. Med. **259**: 581, 1958.

Thirty-two patients, ranging in age from 20 to 54 years, were given benzathine penicillin G, 1,200,000 units intramuscularly every 4 weeks over an average period of 14 months as part of a rheumatic fever prophylaxis program. Allergic reactions were observed in 6 of the 32 patients treated; all these patients had had procaine penicillin previously without any reaction, and only

one had any history of allergy (mild hay fever). In 2 of these patients the reaction consisted of a pruritic eruption which occurred after the fourth and tenth injections, respectively; another patient developed a pruritic eruption and edema of the lips after an injection of aqueous penicillin, although she had received benzathine penicillin G for one year without ill effect; and 2 patients developed a serum sickness type of reaction after the first and second injections of benzathine penicillin G, respectively. The sixth patient, a 54-year-old woman with congestive heart failure and episodes of rheumatic heart disease activity, died within a few minutes following the twentieth injection of benzathine penicillin G. She was treated with epinephrine by the intravenous and intracardiac routes and with oxygen to no avail. An electrocardiogram showed ventricular fibrillation. At autopsy there was evidence of aortic valvular disease and chronic passive congestion of the liver, but there was no evidence of coronary artery disease or pulmonary emboli. Blood was not drawn for circulating penicillin antibody.

The authors conclude that the benefits of a penicillin prophylaxis program have to be weighed against the possible hazards which were demonstrated in this series by the occurrence of one death and 5 other allergic reactions in 32 patients, an incidence of 18.7 per cent. D. Gitlin.

Otorhinology and Ophthalmology

Transillumination of Paranasal Sinuses. McGovern, F. H.: J. A. M. A. **167**: 1620, 1958.

The results of x-ray examination of the sinuses were compared with the findings on transillumination in 100 patients with symptoms referable to the sinuses. The transilluminator was placed behind the lower rim of the orbit and the palatine light reflex was noted through the open mouth. The intensity of the illumination was varied by means of the rheostat on the battery handle. In 3 out of 23 adult males, there was no correlation between x-rays of the sinuses and transillumination. No correlation was found in 22 of 55 cases among women or in 14 of 22 cases among children. These figures were considered by the author to substantiate a long-held estimation of the limited value of transillumination. A surprising number of women and children in this series presented a masked sinusitis, in which the entire clinical examination was negative and the diagnosis was made by x-ray studies and antral irrigation. Transillumination of the paranasal sinuses was therefore regarded as a confirmatory or supplementary test, which has more reliability in men than in women and children in whom only a positive test can be regarded as significant. M. C.

Pharmacology, Physiology, and Pathology

Transport of Epinephrine and Norepinephrine in Human Plasma. Antoniades, H. N., Goldfien, A., Zileli, S., and Elmadjian, E.: Proc. Soc. Exper. Biol. & Med. **97**: 11, 1958.

Bloods were collected either in ACD solution or through cationic exchange resins in the ADL-Cohn blood fractionator. The separated fractions, precipitates I, II, and III, IV-1, IV-4, and V, were resuspended in the smallest possible volume of 0.15 M sodium chloride and subjected to limited dialysis. The fractions were then tested both chemically and biologically for the presence of epinephrine and norepinephrine. Bioassay was based on "the quantitative inhibition by the catechol amines of the contraction induced with acetylcholine in an *in vitro* preparation of rat colon and rat uterus."

Epinephrine, which is present primarily in fraction V, is almost completely bound to human plasma protein. Serum albumin is responsible for the binding and transport of the epinephrine. It is possible that a part of the epinephrine may be bound in fraction IV-4. Norepinephrine also binds with albumin in fraction V but is present in sizable quantities in the unbound state. Acid hydrolysis of fraction V results in an increase of both epinephrine and norepinephrine activity, suggesting the release of these substances from a conjugated form. H. Stryker.

A Comparative Study of Intrapulmonary Gas Mixing and Functional Residual Capacity in Pulmonary Emphysema, Using Helium and Nitrogen as the Test Gases. Hickam, J. B., and Frayser, R.: J. Clin. Invest. **37**: 567, 1958.

Subjects breathed a 50 per cent helium–50 per cent oxygen mixture for 15 minutes. They were then switched to tank oxygen and the air that they expired was analyzed for helium content continuously, the results being plotted against time. A similar procedure was followed using nitrogen instead of helium. The method of Darling was also applied for comparison. Results were tabulated for 11 normal and 21 emphysematous subjects. Substitution of nitrogen for helium made no difference, either in functional residual capacity or in the apparent characteristics of the slowly ventilated lung spaces of emphysematous patients. Gas diffusibility did not appear to be a limiting factor in ventilation of the slowly ventilated lung regions in pulmonary emphysema. A higher mean value of functional residual capacity was found in emphysema patients by the helium method than by the Darling method. The two methods gave good agreement in normal subjects. E. K.

The Measurement of the Pulmonary Diffusing Capacity in the Presence of Lung Disease. Bates, D. V.: J. Clin. Invest. **37**: 591, 1958.

Detailed analysis of the various means currently used to estimate pulmonary diffusing capacity is presented. The unattainable ideal would be the sum of the individual diffusing capacities for each alveolus. The pitfalls of various techniques are discussed. The author favors a "steady state carbon monoxide method" as the simplest procedure to use. It was found that in asthma a mixing defect and a ventilatory defect might be considerable, whereas results of tests for diffusing capacity might be normal at rest. In emphysema, ventilatory function can remain close to normal with regard to evenness of gas mixing and yet diffusing capacity might be frankly abnormal. The use of carbon monoxide in an end-tidal sampling technique in asthma and emphysema "enables an estimate to be made of the relative normality of the lung parenchyma. . . . In patients with pulmonary disease it makes little difference to the calculated D_{CO} on exercise whether the Bohr equation be used to calculate the mean alveolar co, or whether an end tidal sample be taken. This correspondence applies equally to patients with normal and abnormal gas distribution in the lung. Secondly, there is a close relationship between the rate of uptake of Co and the D_{COII} on exercise, and the rate of uptake alone might be used as a test of normality of the lung." E. K.

Pressor Effect of Histamine in the Rabbit. Naranjo, P., and deNaranjo, E. B.: J. Pharmacol. & Exper. Therap. **123**: 16, 1958.

In the anesthetized rabbit small doses of histamine sometimes produce a transient fall in blood pressure. Larger doses "uniformly produced a sharp and marked rise of blood pressure." This was followed by a depressor phase.

Epinephrine given 3 to 5 minutes prior to histamine diminished or reversed the pressor action of histamine. Adrenergic blocking agents Regitene and dihydroergotamine had no effect on the pressor response to histamine but prevented reversal of the temporary hypertension resulting from histamine administration. Ganglionic blocking agents Hexamethonium and Pendiomide increased the pressor effect of histamine and diminished the subsequent depressor reactions. These blocking agents also prevented the antagonism of histamine and epinephrine, so that when these drugs were given together the pressor effect was greater than from either drug alone. Adrenalectomy had no effect on the pressor response to histamine. Anesthesia of progressive depths could be correlated with increasing pressor responses to epinephrine. It is concluded that "in the rabbit, histamine induces a pressor response for which mobilization of epinephrine is not a prerequisite." The results obtained favor the viewpoint that factors causing decreased capillary tone enhance histamine pressor response. E. K.

Mast Cells, Histamine, and Serotonin. Studies of the Human Spleen. Ende, N., and Cherniss, E. I.: Am. J. Clin. Path. **30**: 35, 1958.

A splenectomy was performed on a patient who complained of periodic flushing and tachycardia associated with anemia, leukopenia, and thrombocytopenia suggestive of hypersplenism. The symptoms disappeared following surgery. Analysis of the spleen for heparin revealed 57 mcg. per gram of tissue (normal is 8.3 mcg. per gram). The patient's spleen showed as high as 60 mast cells per oil-immersion field. Normal levels of histamine and serotonin in human spleen have not been reported. Seven spleens removed post mortem were examined. Their histamine content ranged from 1.5 to 3.3 mcg. per gram. The spleen from the patient described contained 100 mcg. per gram. Serotonin content in postmortem spleens varied from 0.1 to 1.0 mcg. per gram. The spleen of the hypersplenic patient showed a value of 0.3 mcg. It was concluded that mast cell concentration in the spleen correlates with histamine content but not with serotonin content. E. K.

Adrenaline and Noradrenaline Content of the Adrenal Gland of the Rat Following Depletion With Reserpine. Callingham, B. A., and Mann, M.: Nature **181**: 423, 1958.

Rats were injected subcutaneously with reserpine (1 mg./Kg.) daily for three days, and control rats were given the solvent only. They were sacrificed at 3, 7, 14, 21, and 28 days following the first injection. The adrenaline and noradrenaline contents of the extracts of the adrenal glands were determined biologically.

At 3 days, the reserpine caused a similar loss (about 50 per cent) of adrenaline and noradrenaline. Following the depletion, the adrenaline content slowly returned to its initial nondepleted value in 21 days and remained at this level. In contrast, noradrenaline increased to several times its original value by the seventh day and then decreased to its original value in 21 days. The authors consider this as evidence that noradrenaline is a precursor of adrenaline in the rat and that the rate of methylation of noradrenaline to adrenaline is slower than the rate of formation of noradrenaline. I. G.

Immunology

Mass Immunization With Monovalent Influenza Virus Vaccine. Katz, M. E.: Antibiotic Med. & Clin. Therapy **5**: 526, 1958.

A dose of 1 ml. (200 C.C.A. units) of monovalent influenza virus vaccine was given subcutaneously to 500 women between the ages of 18 and 70 years

who were employed in an industry. Only one person developed an immediate allergic reaction. This reaction consisted of generalized urticaria and responded to an injection of epinephrine. General aches and pains occurred on the following day in several persons. A significant number of workers complained of soreness at the site of injection, which lasted about 24 hours. There were no instances of absenteeism attributable to the vaccine. M. C.

The Antigenic Role of the Excretions and Secretions of Adult Trichinella Spiralis in the Production of Immunity in Mice. Chipman, P. B.: J. Parasitol. **43**: 593, 1957.

Adult living *Trichinella spiralis* were obtained and incubated in culture fluid for two days. The culture fluid, containing excretions and secretions of the worms, was separated from the worms and used to immunize mice. The mice were subsequently challenged with *T. spiralis* infection. Immunizing doses were administered intraperitoneally every third day. "Twelve injections were required to demonstrate a reduction in the number of adult worms, whereas a reduction in the number of larvae was noted after both 6 and 12 injections." It was concluded that the adult form of *T. spiralis* contributed to host immunity as well as the preadult forms reported in earlier researches. E. K.

Investigation on the Occurrence of Blood Group Antigens in Spermatozoa From Man, and Serological Demonstration of the Segregation of Characters. Gullbring, B.: Acta med. scandinav. **159**: 169, 1957.

Sperm plasma is known to contain A and B red cell substances in persons who are of these blood group types. Spermatozoa washed to remove sperm plasma do not agglutinate with sera containing blood group antigens. When red cells were mixed with spermatozoa, however, a distinct mixed agglutination was obtained. With this technique, antigens A and B have been demonstrated in spermatozoa. In persons of blood group AB, both A and B characters were found in spermatozoa. In the Rh system, antigen D has been identified in spermatozoa. E. K.

Miscellaneous

Neurologic Manifestations of Chronic Pulmonary Insufficiency. Austen, F. K., Carmichael, M. W., and Adams, R. D.: New England J. Med. **257**: 579, 1957.

A syndrome consisting of the symptoms and signs of pulmonary and cardiac failure, associated with headache, papilledema, impairment of consciousness, and tremor and twitching of the extremities is described. Chronic pulmonary insufficiency was the underlying disorder in each case, but the causative factor of the insufficiency varied in each patient. It was due to thoracoplasty, bronchial asthma, chronic bronchitis, or kyphoscoliosis. Congestive heart failure, left- as well as right-sided, was present in each case. Headache was a prominent symptom in two of the four cases described. Papilledema, which was present in three of the four patients, could not be distinguished from papilledema due to other causes of increased intracranial pressure. It varied from a slight blurring of the disc margins to choking, with marked venous congestion and peripapillary hemorrhages. Impairment of consciousness, drowsiness, inattentiveness, disorientation in time and place, tremor, and twitching of the extremities were present in each of the four patients. Tremor was visible only in the outstretched

fingers and had all the characteristics of an action tremor. Twitching movements resulted from the inability to maintain a fixed posture and were observed whenever muscles were activated and maintained in a state of contraction. Electroencephalographic tracings, made both before and after treatment, showed an abundance of activity in the slower frequency ranges in all leads. These findings were present in three of the four patients. It was suggested that papilledema was due to pulmonary insufficiency associated with heart failure with pulmonary congestion and an acute increase in venous pressure. The aggravation of the existing hypoxia and hypercapnia produced congestion of the brain, which in turn was responsible for the development of papilledema. Elevation of carbon dioxide tension in the blood stream was regarded as the main factor responsible for drowsiness and impairment of consciousness. The mechanism of the varying types of headaches could not be correlated with the degree of hypoxia, hypercapnia, or elevation of spinal-fluid pressure. Because the headaches were sometimes aggravated by oxygen administration, carbon dioxide retention with increased cerebral blood flow was thought to play the major part in their development. The exact mechanism for the production of tremor and twitchings remained obscure. The therapeutic program that completely reversed the neurologic disturbance in three of the four patients was directed toward the restoration of cardiac and pulmonary compensation. E. W.

Effectiveness of Triacetyloleandomycin in a Wide Variety of Infections. Wennersten, J. R.: Antibiotic Med. & Clin. Therapy **5**: 527, 1958.

Triacetyloleandomycin (Tao), a new antibiotic found in the laboratory to be considerably better absorbed than its precursor, oleandomycin, was given to 135 patients with a wide variety of infections. It was administered in capsules of 125 and 250 mg. each, according to the age of the patient and the type of illness. The latter included acute pharyngitis, tonsillitis, bronchitis, pneumonia, pleurisy, furunculosis, cellulitis, otitis media, and acute sinusitis. A very prompt clinical response and complete recovery occurred in 120 patients (89 per cent), an adequate clinical response was noted within a short time in 12 patients, and in 3 patients there was no response. As part of the initial evaluation of this drug, the offending microorganism was isolated in a series of 20 patients. Excellent responses were obtained against the following bacteria: *Staphylococcus albus* and *S. aureus;* beta-hemolytic, hemolytic, and nonhemolytic streptococci; gonococcus; pneumococcus; and *E. coli.* Triacetyloleandomycin was very well tolerated. Mild side effects were observed in only seven instances. M. C.

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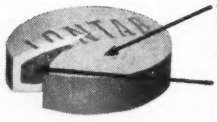

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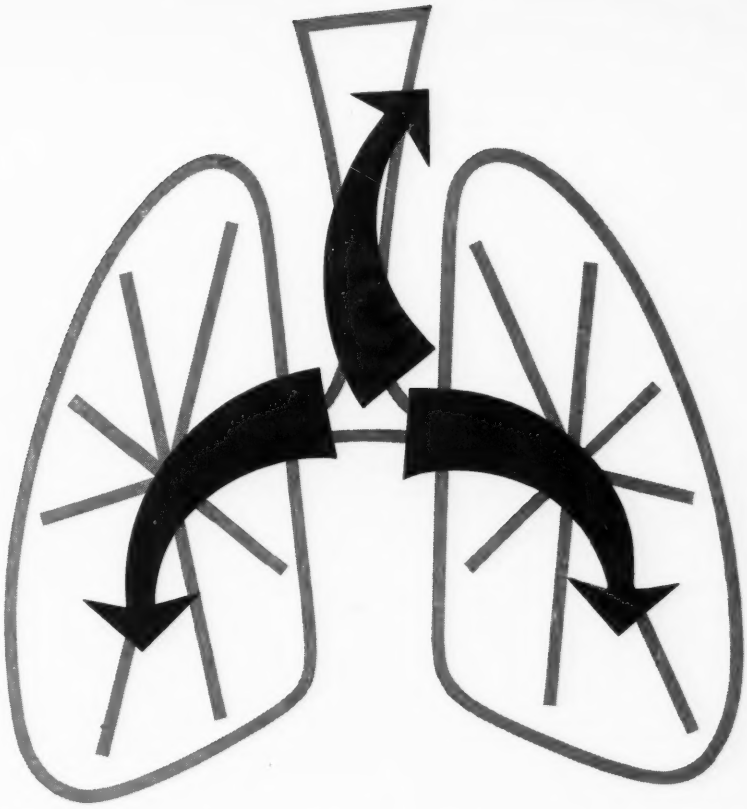

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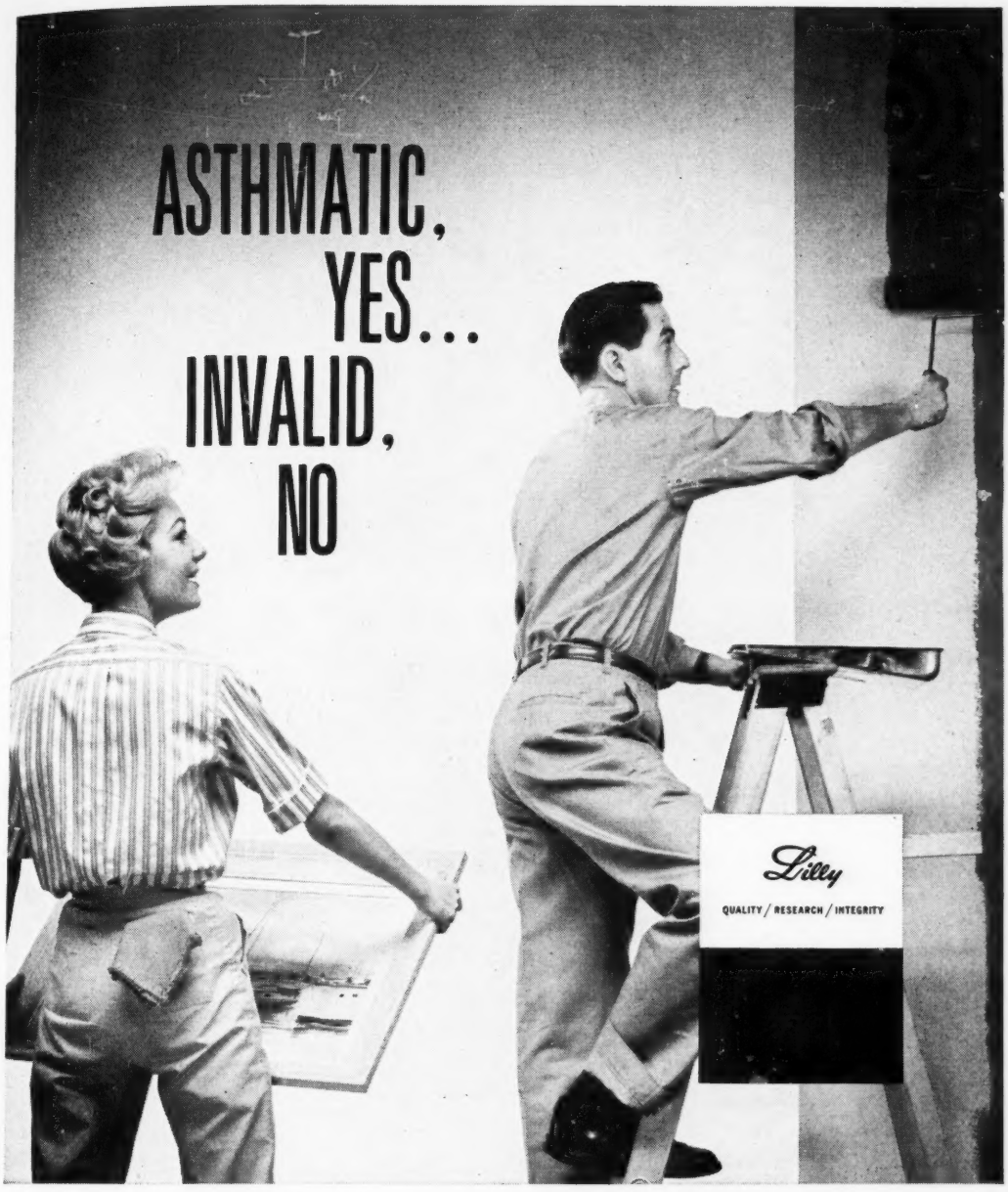

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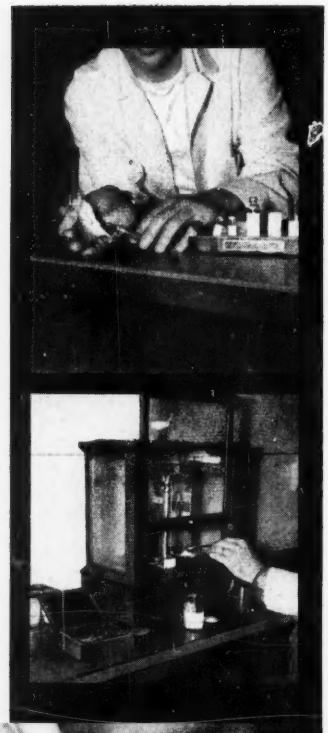

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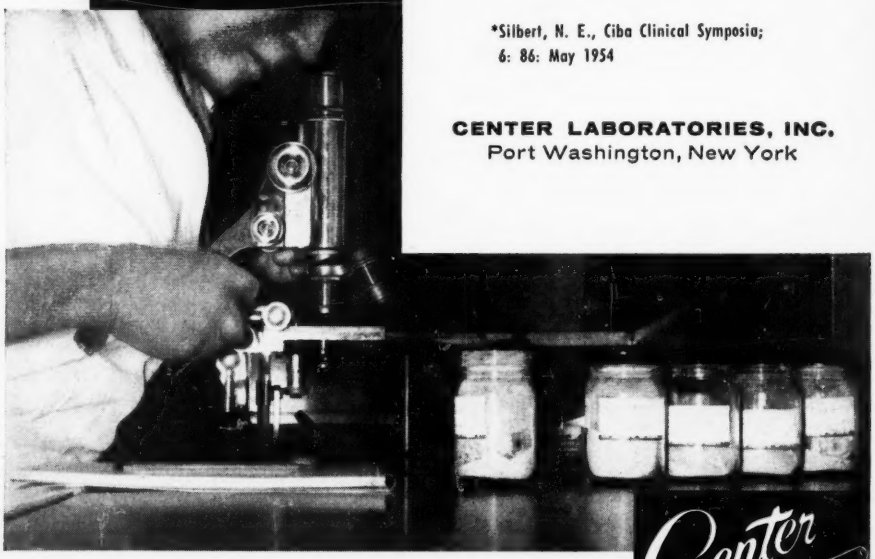

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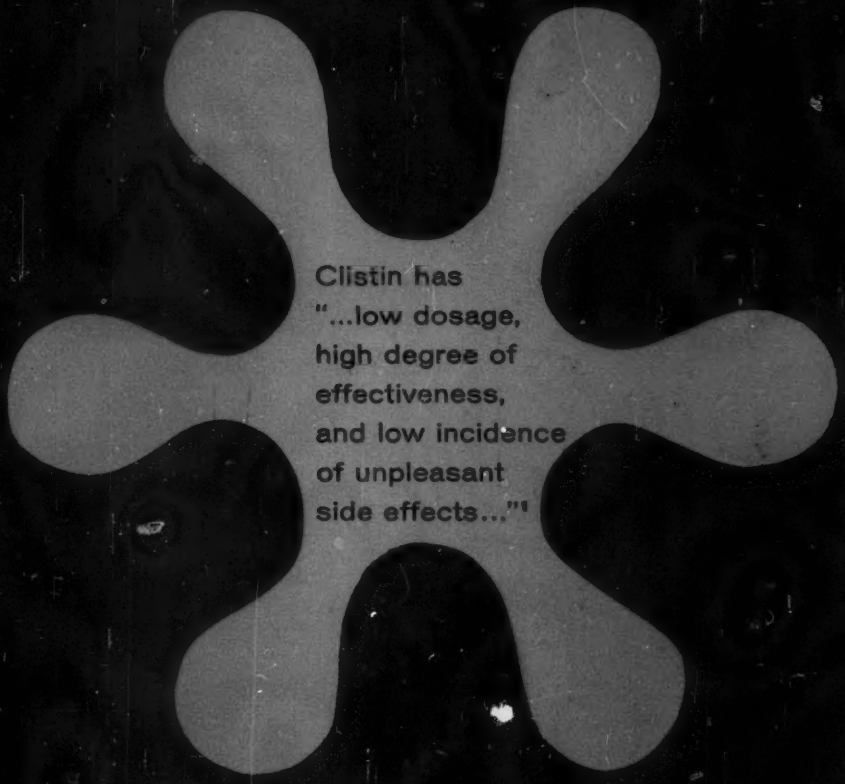

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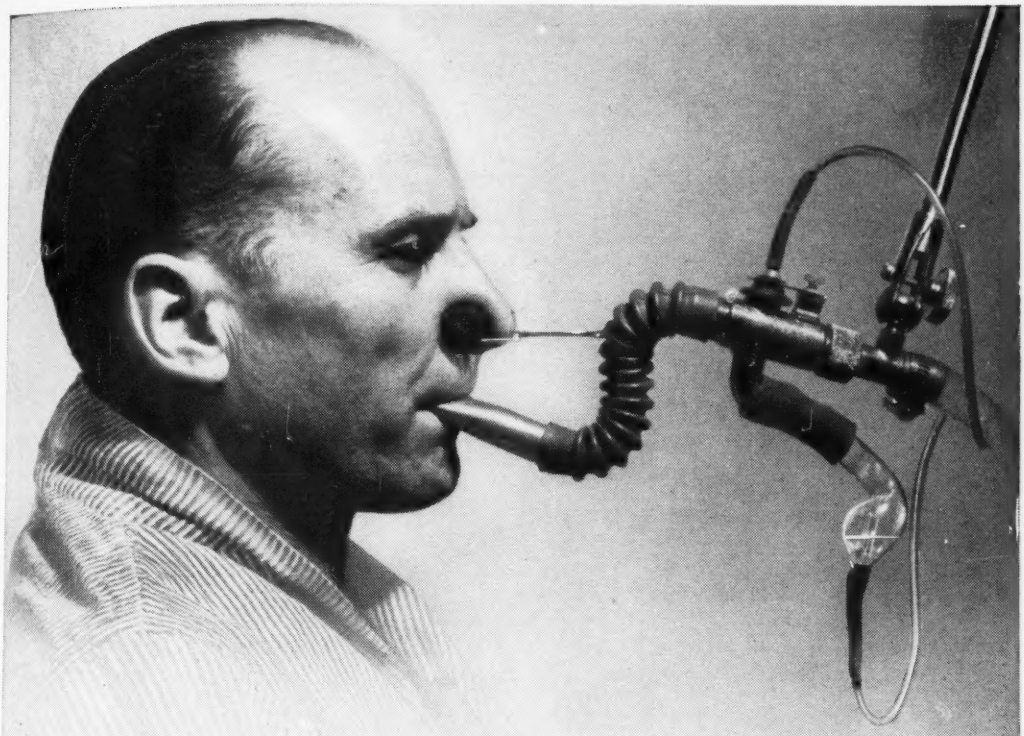

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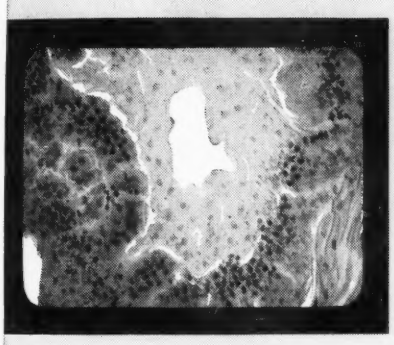

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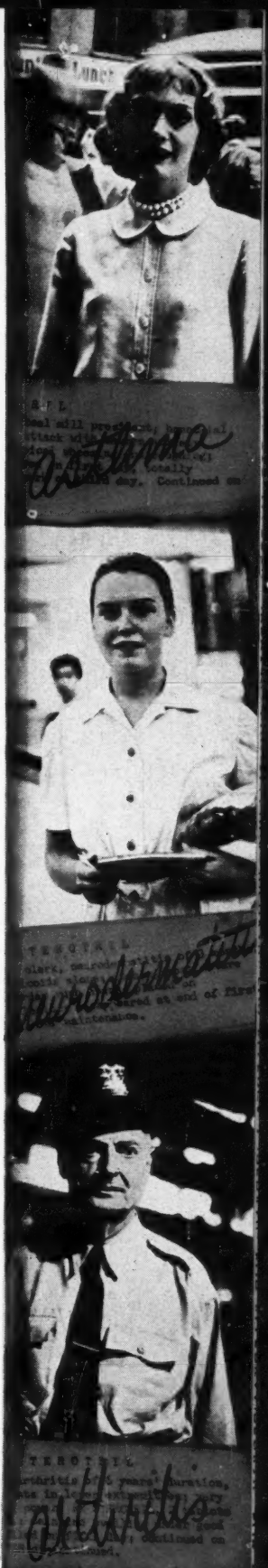

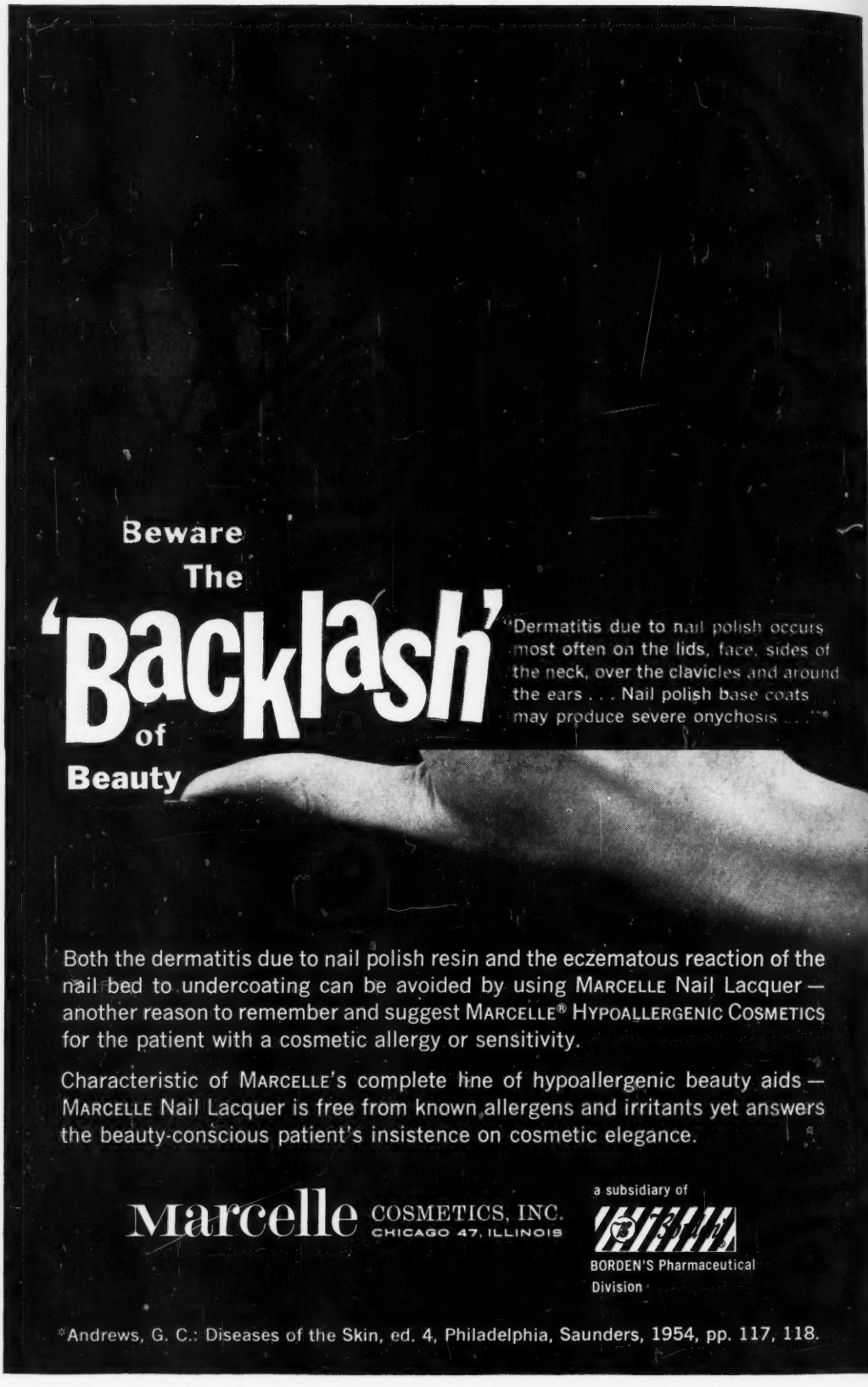
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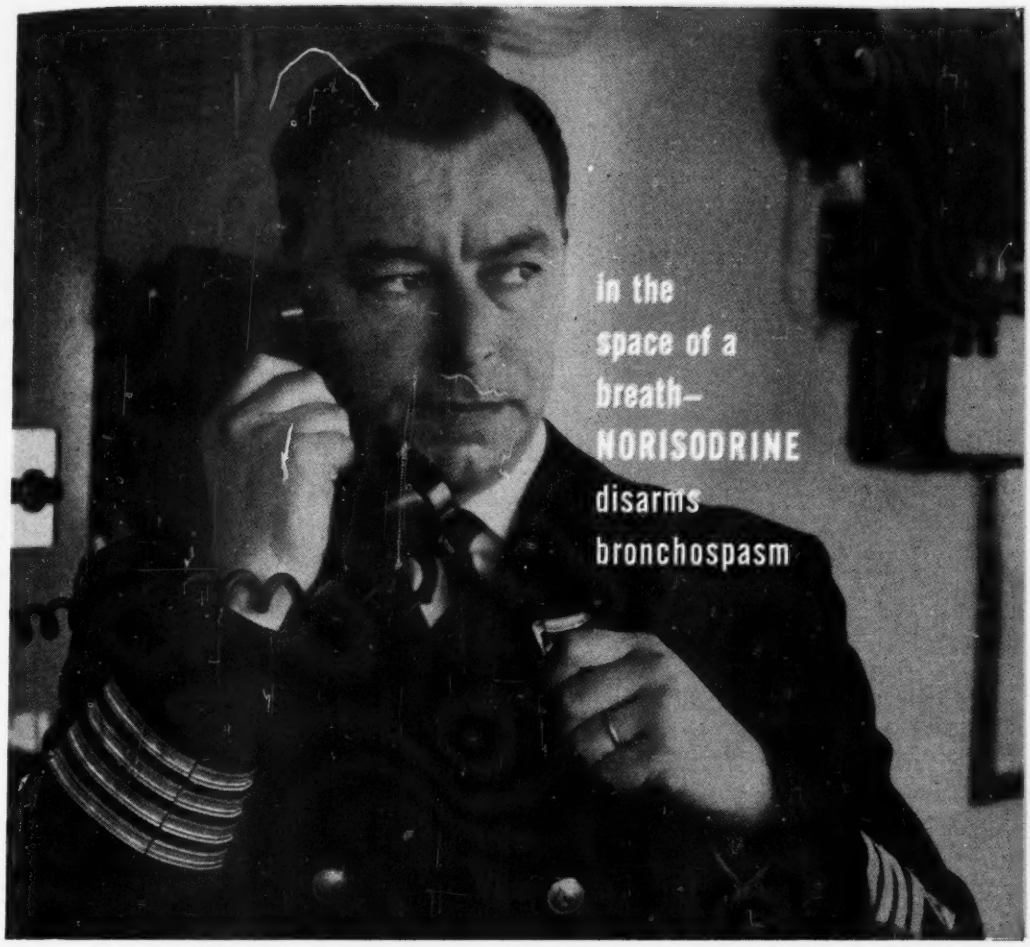

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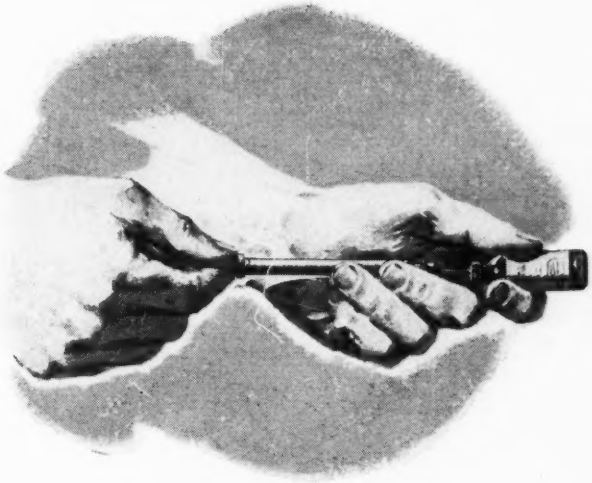

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1. Levin, S.: J. Ped. Clin. of N.A., 1:975 (1954).
2. Naterman, H.L.: J. of Allergy, 20:64 (1953).
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4. Jenkins, C.M.: J. Nat. Med. Assn., 45:120 (1953).

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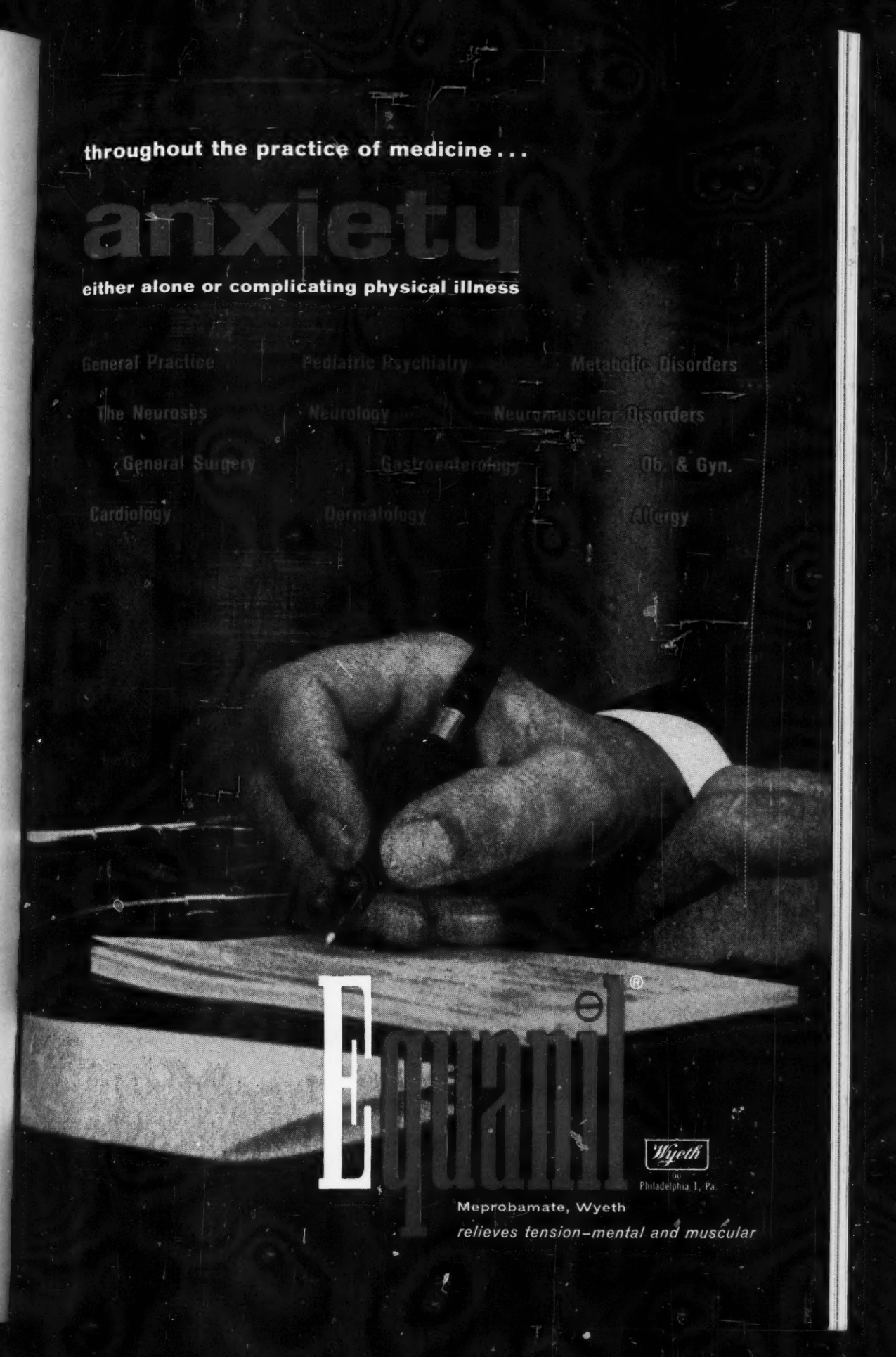

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1. Howell, C. M., Jr.: Am. Pract. & Digest Treat. 8:1928, 1957.
2. Frank, L.: A.M.A. Arch. Dermat. 75:876, 1957.
3. Welsh, A. L.: Internat. Rec. Med. 169:775, 1956.
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Except for the title there is very little similarity between this enlarged and expanded edition of "PRACTICE OF MEDICINE" and the five previous editions. Where the first five editions were almost entirely the work of Doctor Meakins, he has served only as Editor-in-Chief of this edition. Working under him were 24 Associate Editors—and they, in turn, had 87 contributors do most of the actual writing. As a result the book is entirely new and different.

Designed to assist the practitioner of medicine in solving the numerous puzzles and problems which he daily encounters, this book is arranged according to diseases of the various systems and organs—a plan that lends itself to simplicity. It is eminently a clinical book with symptoms being given particular prominence. The pathological basis of symptoms is everywhere stressed, and the bedside recognition and interpretation of clinical signs is described with a sustained interest and lucidity rarely found in tomes of this size.

The major responsibility of this revision was placed in the hands of the 24 Associate Editors—each unto his own particular realm; each with a broad understanding of the unity of medicine as a whole; each realizing that the wide subject of man's disabilities could not be viewed as made of segregated entities, but that there must be coordination of the anatomic, physiologic, emotional, and environmental whole.

In each section where applicable, reference to the so-called psychosomatic patterns and psychologic aspects has been made, and there is, finally, a section on Psychosomatic Medicine, designed to knit the general concepts of this branch into an integrated whole.

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Distinguished
for THERAPEUTIC SAFETY

In hay fever, the corticoid effectiveness and therapeutic safety of Medrol were amply demonstrated in a double-blind study of 131 patients.† These were divided into 3 groups—those treated with Medrol, those given equal doses of prednisolone, and the controls, treated with nonsteroid drugs.

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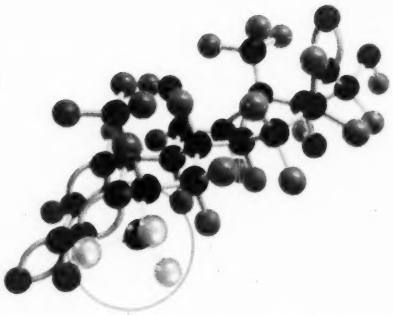

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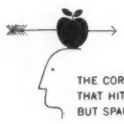

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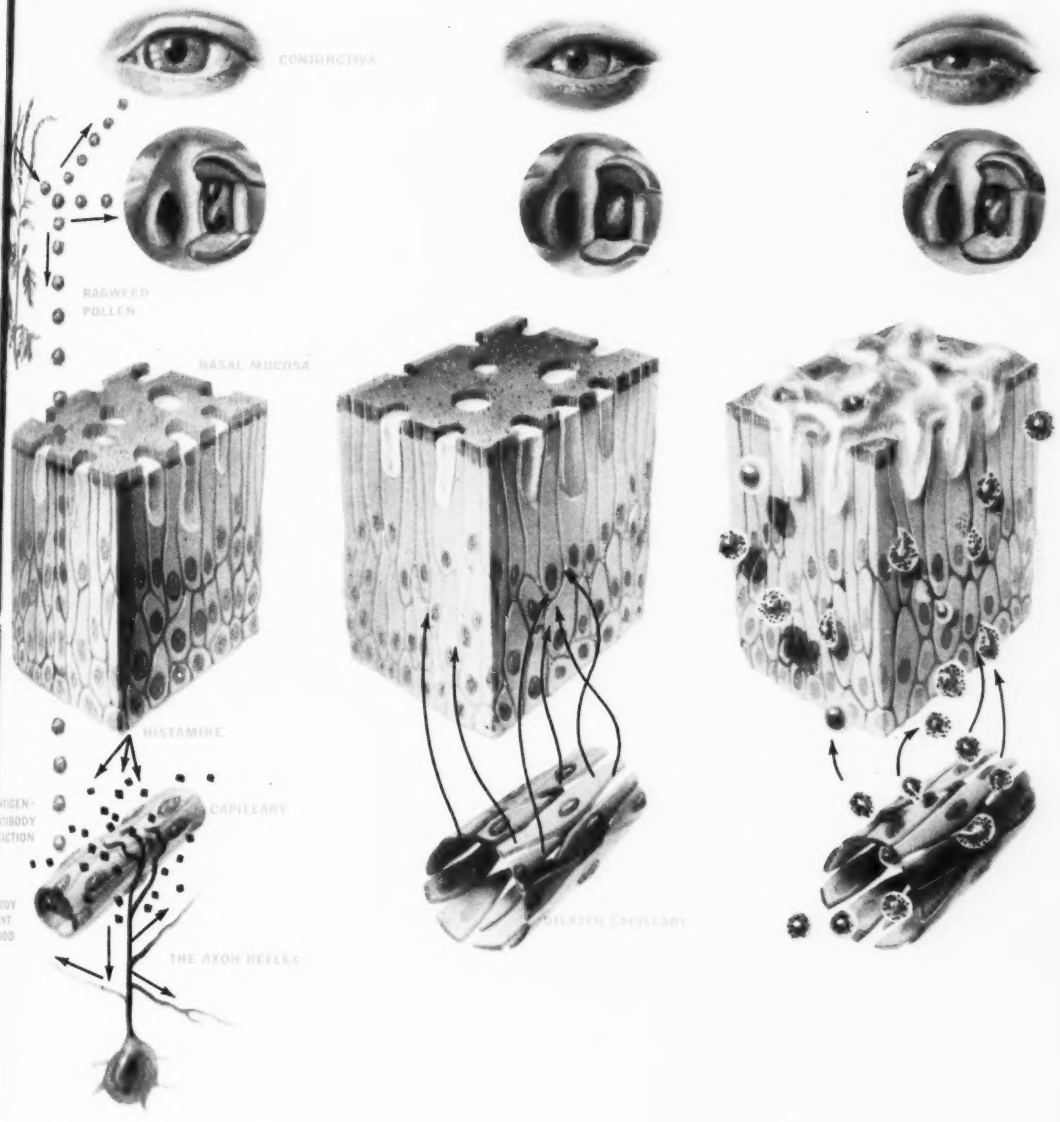
Pollen, after entering blood stream of the allergic patient, initiates the antigen-antibody reaction, with resulting release of histamine. Axon and collateral axons extend local reaction to wider areas of mucosa in the **axon reflex**.

2. THE IMMEDIATE REACTION

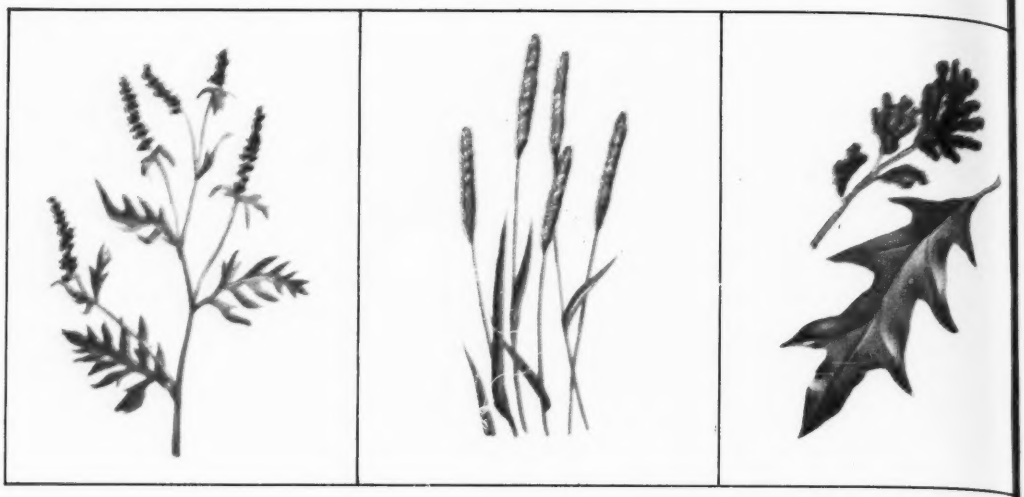
Capillaries and venules dilate, causing **erythema**. Enlarged intercellular interstices of vessel allow exudation of serum and **edema**.

3. CONTINUATION

Continued exposure to the allergen with the concomitant antigen-antibody reaction increases mucus secretion and causes transmigration of eosinophiles.



IN HAY FEVER Medrol



Some of the most common causative factors in hay fever are pollens of the **short ragweed, timothy grass,** and **pin oak.**

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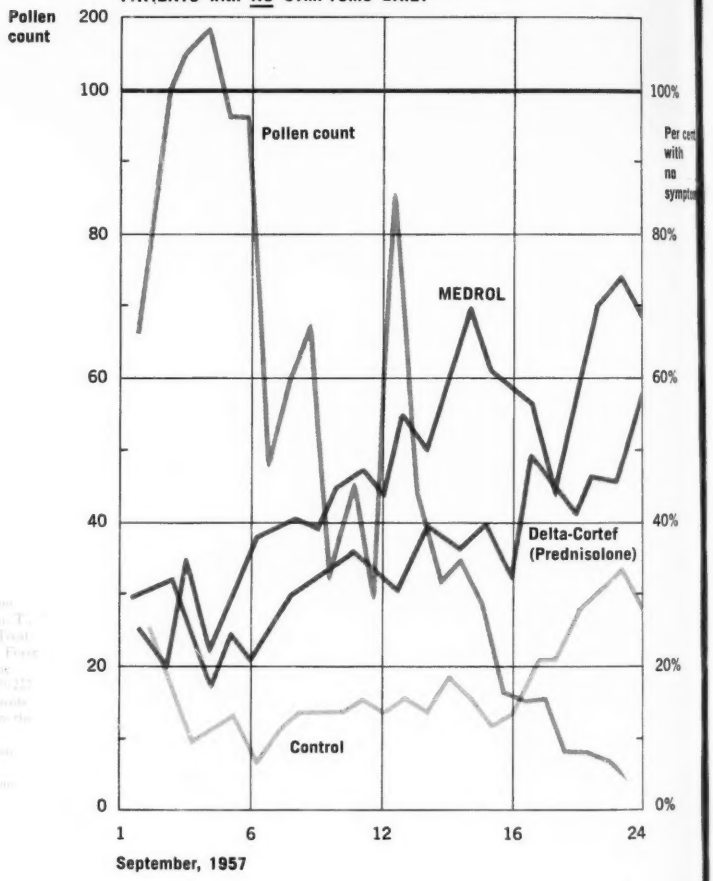
PATIENTS with NO SYMPTOMS DAILY



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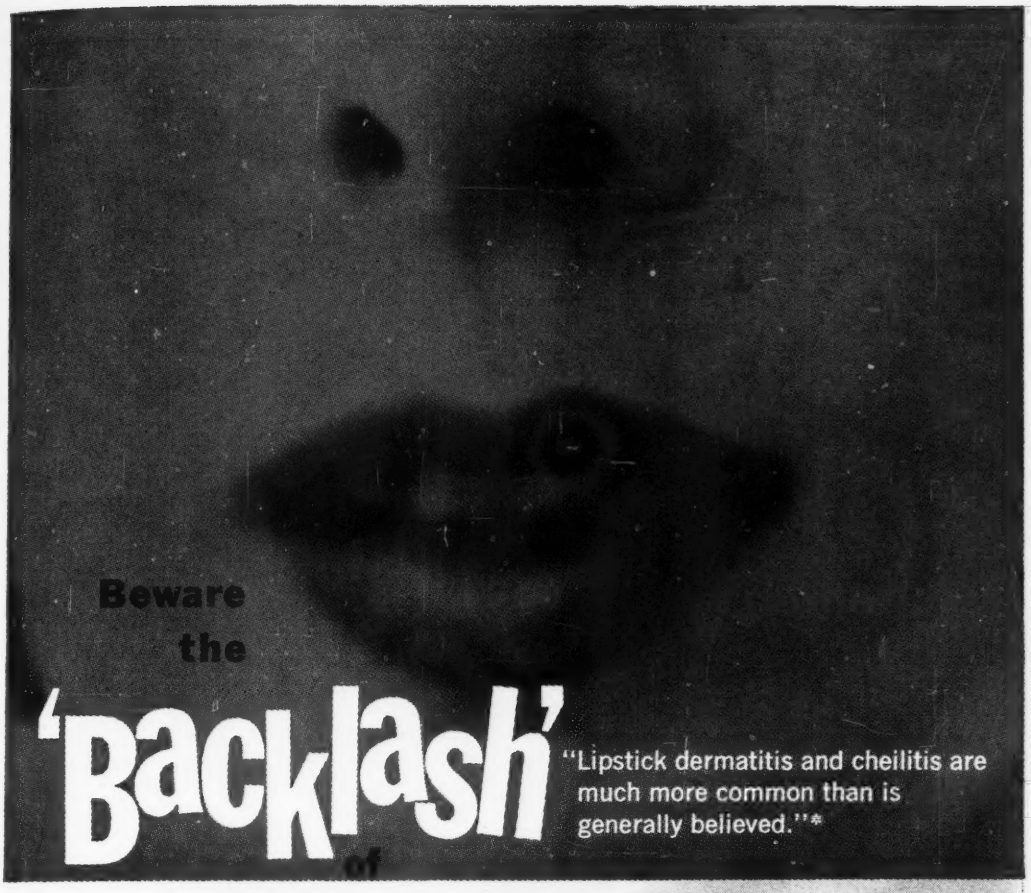

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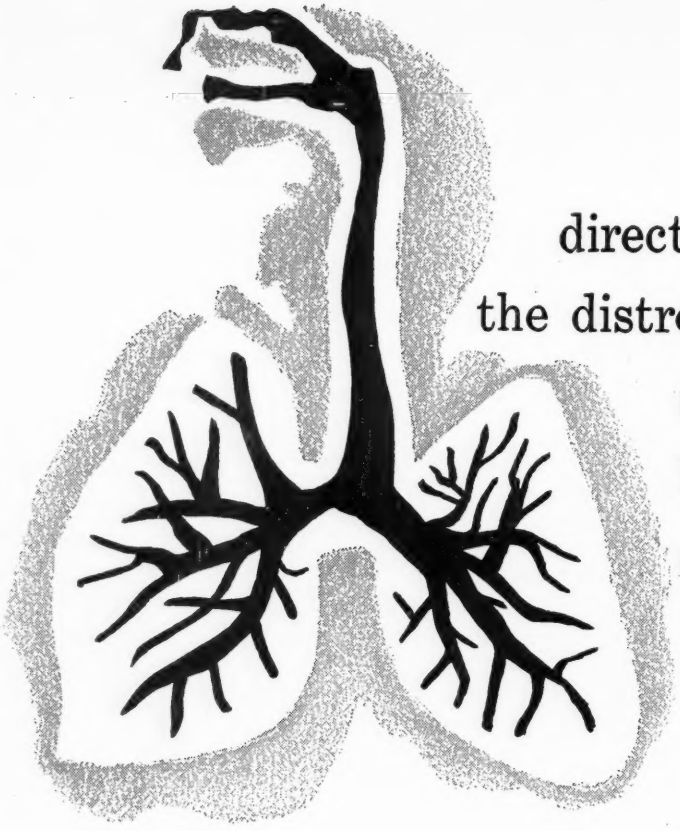

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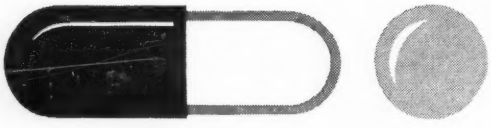

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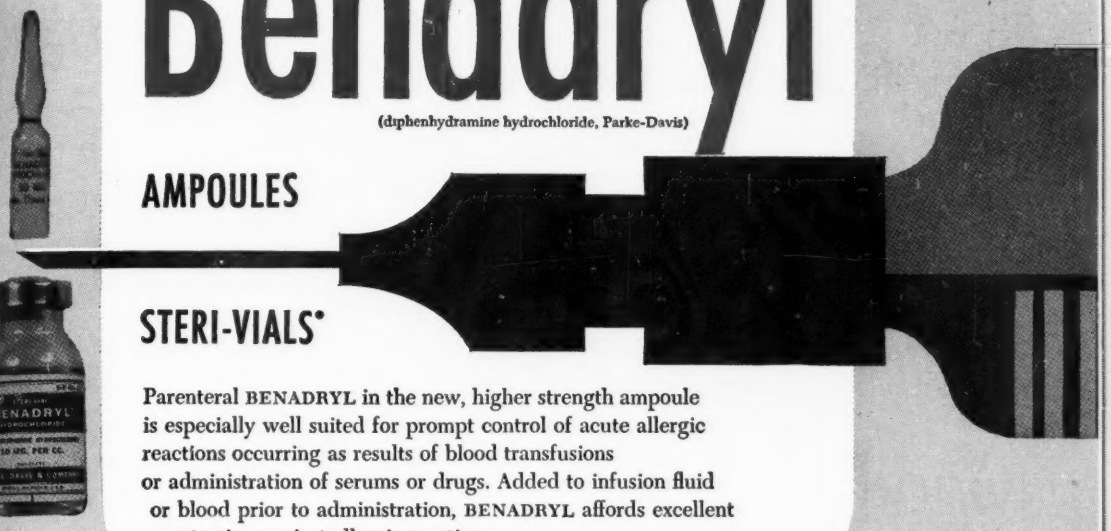

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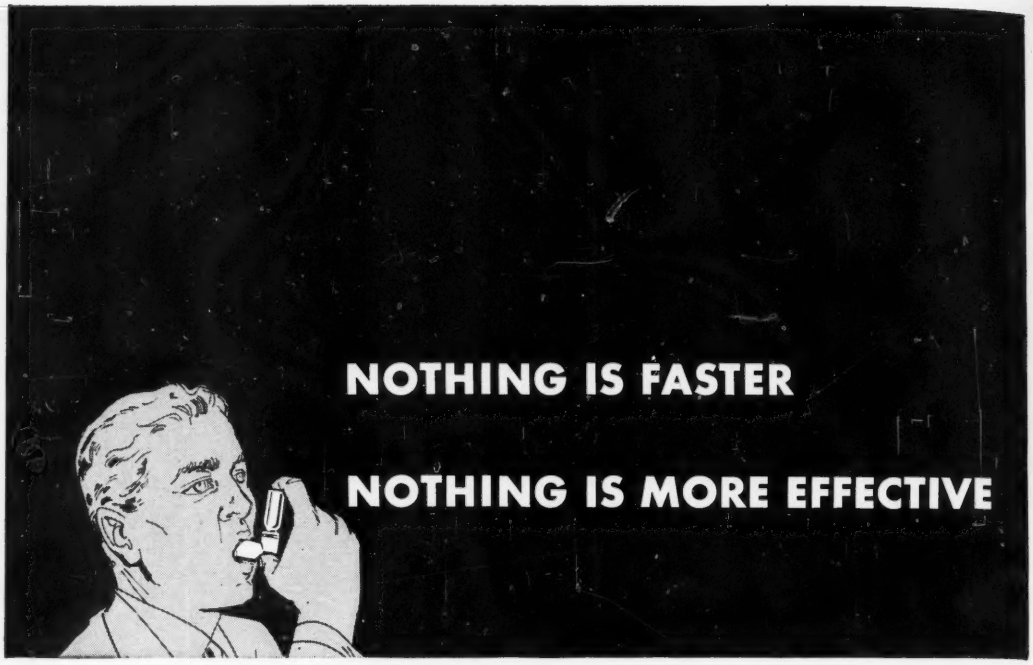

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R. M. Becker, Antibiotics Annual 1957-58.[1]

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references: (1) Becker, R. M., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 310. (2) Zimmerman, M. C.: Clin. Med. *5*:305, 1958. (3) Zimmerman, M. C.: J.A.M.A. *167*:1807, 1958.

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3. Dalven, J., and Romano, F. J.: New York J. Med. *57*:1748 (May 15) 1957.
4. Gundy, J. E.: J. Pediat. *51*:516 (Nov.) 1957.
5. Spielman, A. D.: A.M.A. Arch. Otolaryng. *67*:204 (Feb.) 1958.

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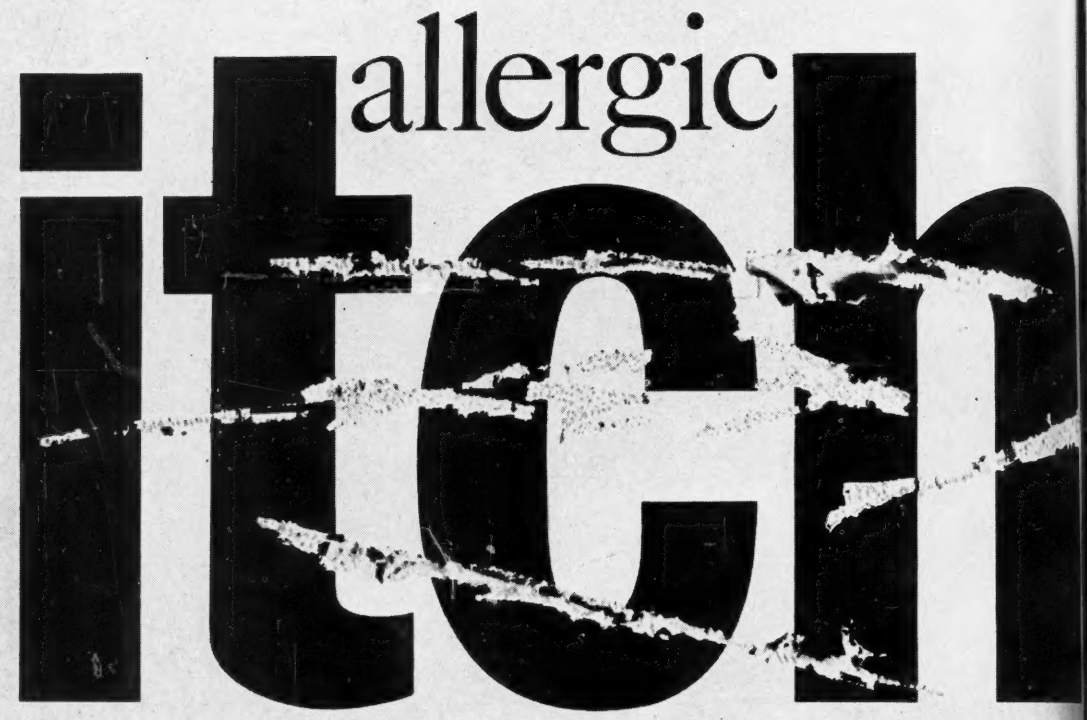

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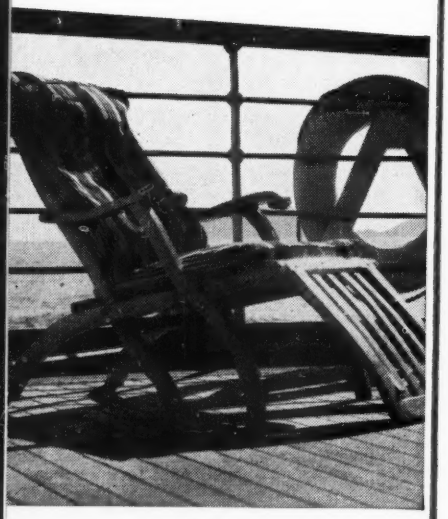

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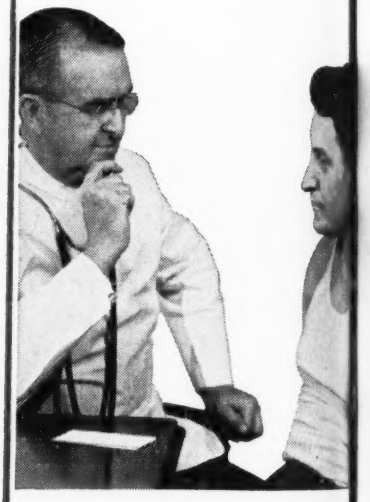

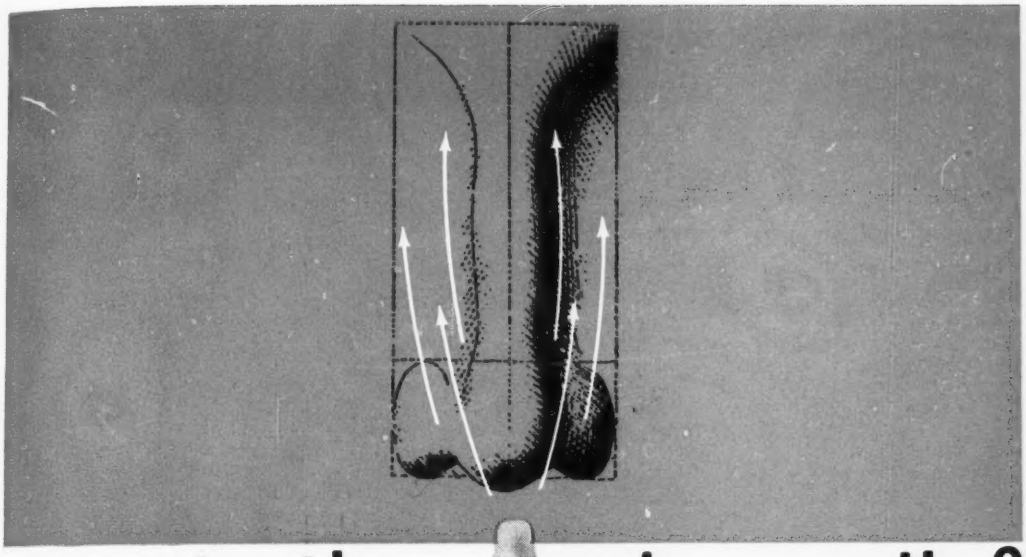

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1. Clayman, S. J.: *J. Med. Soc. N. J.* 55:168 (April) 1958.

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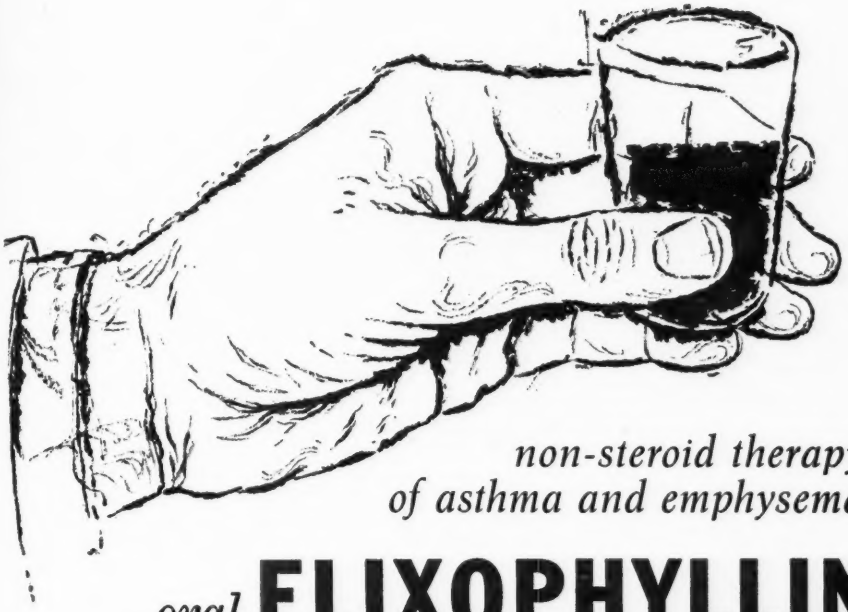

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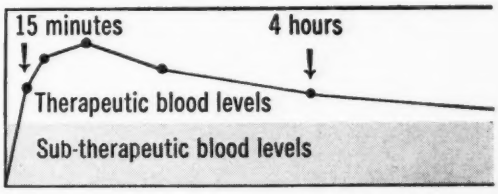

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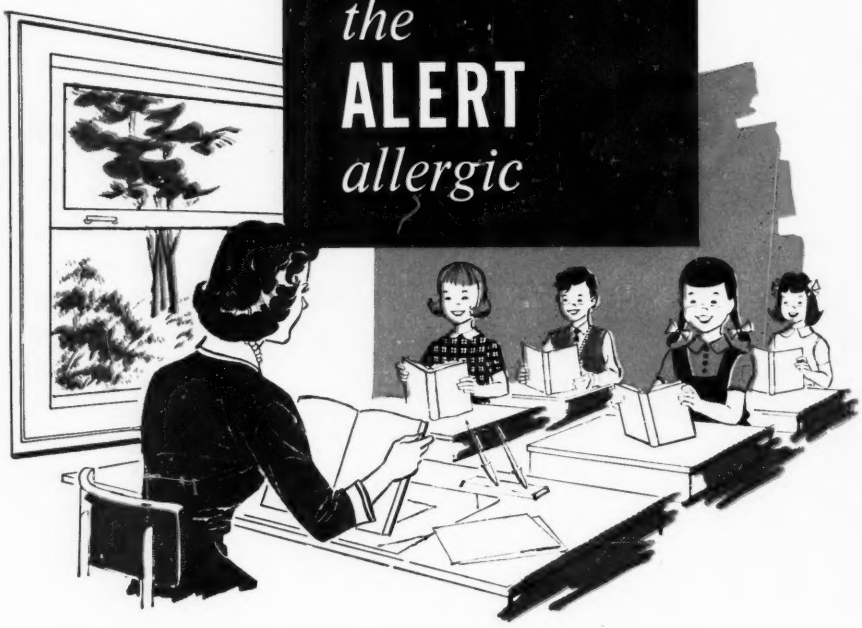

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1. Johnson, H. J., Jr.: Am. Pract. & Digest. Treat. *5*:862 (Nov.) 1954.
2. Beale, H. D.; Rawling, F. F. A., and Figley, K. D.: J. Allergy *25*:521 (Nov.) 1954.

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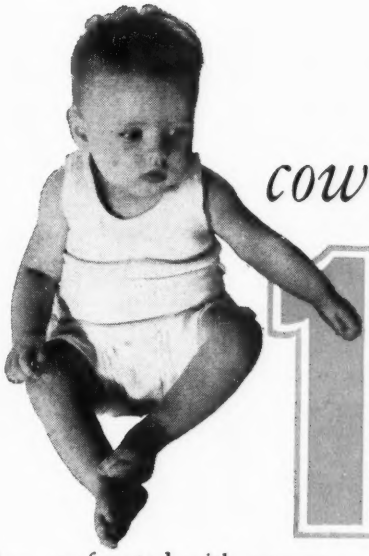

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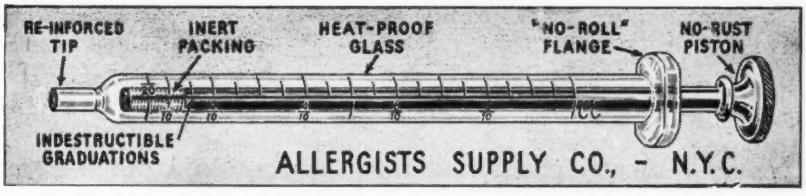

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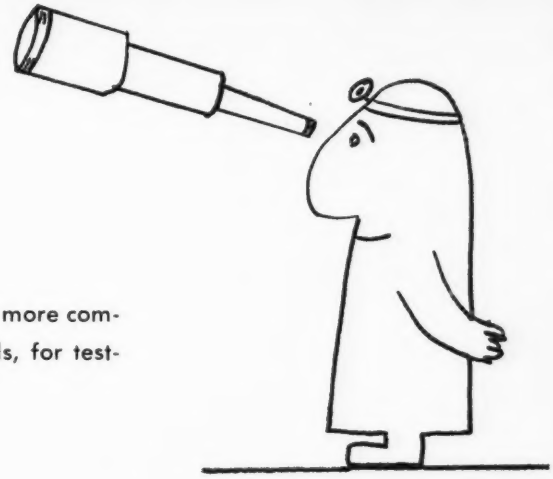

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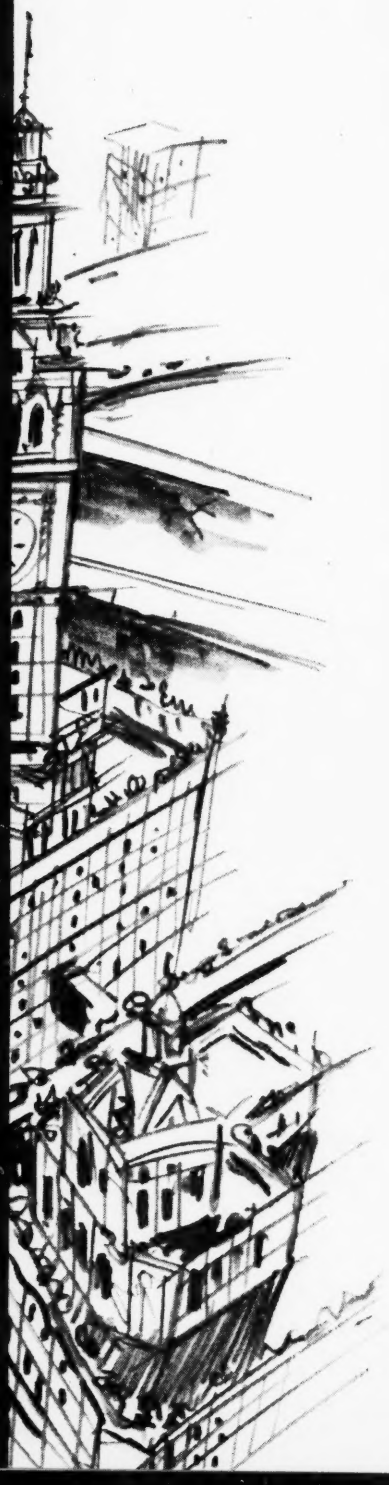

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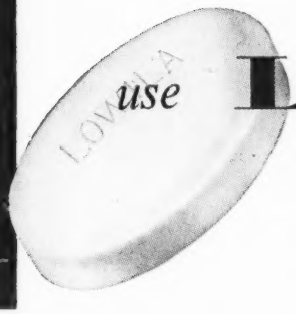

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